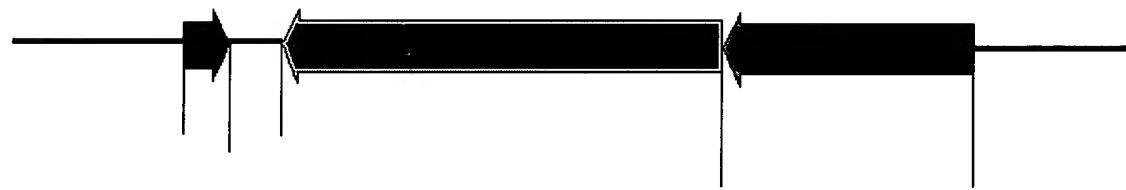




App. No. 09/833,017  
Inventor: Cvitkovitch et al.  
Atty. Dkt: 2224-01301 (formerly 1889-00401)  
Replacement Sheet 1 of 19

Figure 1

**Streptococcus mutans**  
***ComCDE Operon***



**Figure 2A.**

[ATGAAAAAAACACTATCATTAAAAAATGACTTTAAAGAAATTAAGACTGATGAATTAGA  
GATTATCATTGGCGGA (AGCGGAAGCCTATCAACATTTCCGGCTGTTAACAGAAGTT  
TTACACAAGCTTGGGAAAA) ] TAA

**Figure 2B.**

AGCGGAAGCCTATCAACATTTCCGGCTGTTAACAGAAGTTAACAGCTTGGAA  
AAA

**Figure 2C.**

[ATGAATGAAGCCTTAATGATACTTCAAATGGTTATTAACCTATCTAACCGT  
TCTATTCTCTGTTCTATTTCTAAGGTAAAGTAATGTCACTTATCGAAAAAA  
GGAATTAACCTTTTCGATAAGCAATTCTGATAATGATTGCTGTTACGA  
TGGTGAACGTAACCTGTTATCCTGCAGAGCCTCTTATTAGCTTAT  
CAATTATCTTAATAGACAGAATAGTCTTCTAAATATATTATGGTCTGC  
TGCCTGTTGCCAGTTCTGACTTGTTAGGCAGGCAATCATATTCTTATCTGG  
ATGGAACCTAAGGAATTGTAATGGGAGTAGCATTATAACCACCTATGAT  
CGAGTTGCAGGAATAGCGCTAACGTTACCTCTCAGTGTGTTCAATGTTG  
ATATTGGTCGACTAAAGATAAGTTGACCAAGATGAAGGTCAAAACGCTT  
GATTCCAATGAATATTACTATGCTCTACTACCTTTAATACAGGTATTGT  
ATGTTATAGAGAGTTATAATGTGATACCGACTTAAAGTTCTGAAATTGTC  
GTTATTGCTATCTTATTGATTCTGATCTCATTAAAGCCAATATA  
CCAAACAAAAGGTTCAAAATGAGATAATGGCACAAAAGGAAGCTCAGATTG  
GAAATATCACCCAGTATAGTCAGCAAATAGAATCTCTTACAAGGATATTG  
AAGTTCCGCCATGATTATCTGAATATTAACTAGCCTCAGATTAGGCATTG  
AAAATAAAGATTAGCTAGTATTGAAAAGATTACCATCAAATCTTAGAAAAA  
AACAGGACATCAATTGCAGGATACCCGTATAATATCGGCCATCTAGCTAAT  
ATTCAAAACGATGCTGTCAGGGTATCTGTCAGCAAAATCTTAGAAGCTC  
AGAATAAAAAGATTGCTGTCATGTAGAAGTCTCAAGTAAAATACAACGCC  
TGAGATGGAGTTGCTGATTCTGATTACCATACTTCTATCTTGTGATAATGC  
CATTGAGGCTGCTTCAATCATTAAATCCTGAAATTCACTGCTTCTTAA  
AGAAAAATGGCAGTATAGTCTTATCATTCAAGTAAAGAAAATCTTCAACTAAAGGCTCCAAT  
CGCGGTATTGGTTAGCAAAGGTGAATCATATTCTGACACATTCCAAAC  
CAGTTACAAACAAGCAATCATCATCATTATTCAAGCAACTCCTAATAATAA  
AA]TAG

**Figure 2D.**

[ATGATTCTTTGTATTGAAAGATGATTTACAACAAAGGACGTCTGAAACCAC  
CATTGCAGCTATCATGAAAGAAAAATTGGTCTTATAAAGAATTGACTATTTGGAAA  
ACCACAAACAACCTATTGACGCTATCCCTGAAAAGGGCAATCACAGATTTCTTTGGA  
TATTGAAATCAAAAAAGAGGAAAAGAAAGGACTGGAAGTAGCCAATCAGATTAGACAGCA  
TAATCCTAGTCAGTTATTGTCTTGTACGACACATTCTGAGTTATGCCCTCACTTT  
TCAGTATCAGGTATCTGCTTGATTGATAAAATCTTGAATCCTGAGGAGTTCTC  
CCACCGCATTGAATCAGCGCTGTATTATGCTATGGAAAACAGCCAGAAGAATGGTCAATC  
AGAGGAACCTTTATTTCCATTCACTGAAACTCAGTTCAGGTCCCTTGCTGAGAT  
TCTGTATTTGAAACATCTCAACAGCCCATAAGCTCTGCCCTTATACTTATGATGAACG  
GATTGAATTCTACGGCAGTATGACTGACATTGTTAAATGGATAAGAGACTTTTCAGTG  
CCATCGCTTTATTGTCAATCCTGCCAATATTACCCGTATTGATCGGAAAAACGCTT  
GGCCTATTTGAAATAATAAGTCTTGTCTTACGAACTAAGTTAACAAAAGCAG  
AGCTGTGATTGCTGATCAAAGGAGAGCAAA] TGA

Figure 3

A.

MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK

B.

MNEALMILSNGLLTYLTFLFVKSVNTLSKKELTLSFSISNFLIMIAVTMVNVNL  
FYPAEPLYFIALSIYLNRQNQLSLNIFYGLLPVASSDLFRRAIIFFIILDGTQGIVMGSS  
IITTYMIEFAGIALSYLFLSVFNVDIGRLKDSLTKMKVKRRLIPMNITMLLYLLIQVL  
YVIESYNVIPTLKFRKFVVIVYLILFLILISFLSQYTKQKVQNEIMAQEAQIRNITQY  
SQQIESLYKDIRSFRHDYLNILTSRLGIENKDLASITEKLYHQILEKTGHQLQDTRYNI  
GHLANIQNDAVKGILSAKILEAQNKIAVNVEVSSKIQLPEMELLDFTILSILCDNAI  
EAAFESLNPEIQLAFFKNGSIVFIQNSTKEKQIDVSKIFKENYSTKGSNRGIGLAKV  
NHILEHYPKTSLQTSNHHHLFKQQLIICK

C.

MISIFVLEDDFLQQGRLETTIAAIMKEKNWSYKELTIFGKPQQLIDAYPEKGNHQIFFL  
DIEIKKEEKKGLEVANQIRQHNPSAVIVFVTTTHESEFMPLTFQYQVSALDFIDKSLNPEE  
FSHRIESALYYAMENSQNGQSEELFIFHSSETQFQVPFAEILYFETSSTAHKLCLYTY  
DERIEFYGSMTDIVKMDKRLFQCHRSFIVNPANITRIDRKRLAYFRNNKSCLISRTKL  
TKLRAVIADQRRAK

Figure 4

A.

BM71 CSP	1 MKKTPSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK	46
GB14 CSP	1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK	46
H7 CSP	1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK	46
JH1005 CSP	1 MKKTLSLKNDFKEIKTDELEIIIGGSGTLSTFFRLFNRSFTQAA	43
LT11 CSP	1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK	46
NG8 CSP	1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK	46
UAB159 CSP	1 MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK	46

\*\*\*\*\* \*\*\*\*\*

B.

consensus: 1 MKKTLSLKNDFKEIKTDELEIIIGG SGSLSTFFRLFNRSFTQALGK 46  
predicted cleavage site:

Figure 5

SGSLSTFFRLFNRSFTQALGK

Figure 6

### Genetic Transformation in *S. mutans* Biofilms

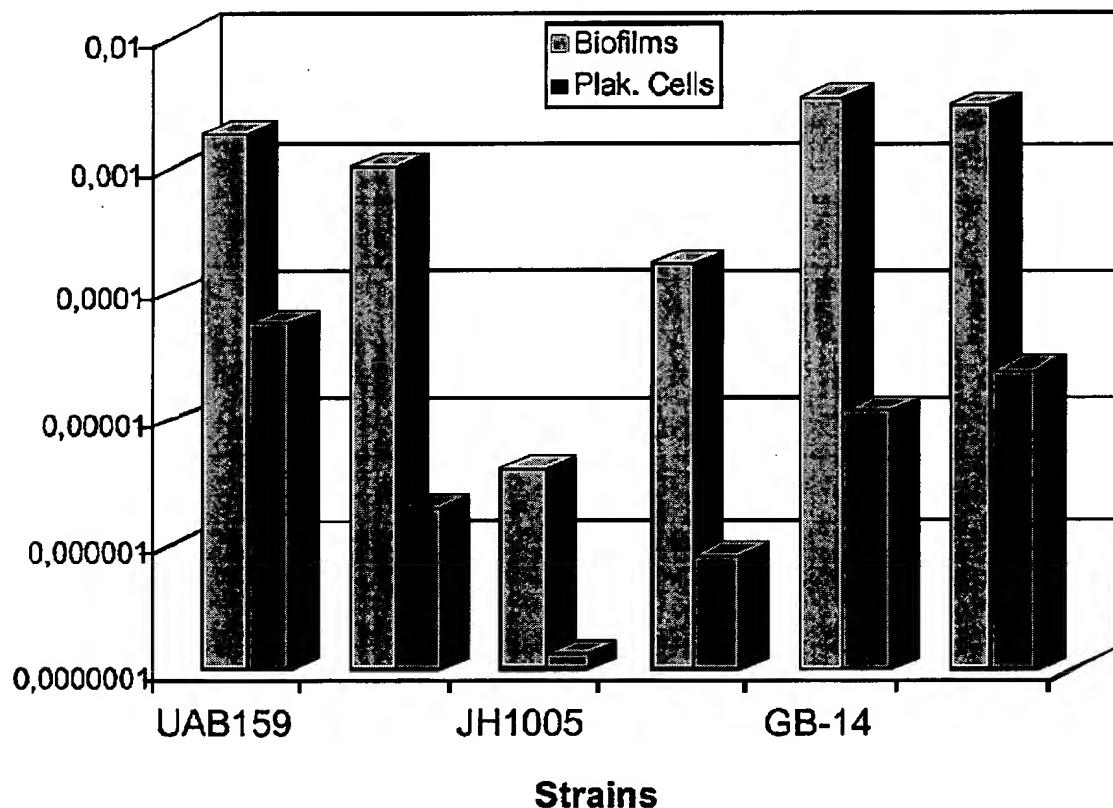


Figure 7

Strain	Peptide added Number of Transformants/Recipients	No peptide Number of Transformants/Recipients
UAB15	$4.65 \times 10^{-1}$	$1.78 \times 10^{-6}$
JH1005 <sup>2</sup>	$6.98 \times 10^{-2}$	0

<sup>1</sup>The final concentration of SCSP used was 500 ng/ml.  
The strain contains a nonsense mutation in the *comC* gene encoding the CSP.

## Figure 8

### ComC region

#### ComC Primer Pair: F5-B5

[F5] 23406-23424 5'- AGTTTTTGCTGGCTGCG -3'

19 nt forward primer

pct G+C: 47.4 Tm: 50.5

[B5] 24056-24037 5'- TCCACTAAAGGCTCCAATCG -3'

20 nt backward primer

pct G+C: 50.0 Tm: 51.9

651 nt product for F5-B5 pair (23406-24056)

Optimal annealing temp: 50.3

pct G+C: 30.9 Tm: 71.5

### ComD region

#### ComD Primer Pair: F1-B1

[F1] 392-415 5'- CGCTAAGTTACCTCTTCTCAGTG -3'

24 nt forward primer

pct G+C: 45.8 Tm: 51.6

[B1] 683-663 5'- GCTTCCTTTGTGCCATTATC -3'

21 nt backward primer

pct G+C: 42.9 Tm: 50.8

292 nt product for F1-B1 pair (392-683)

Optimal annealing temp: 49.5

pct G+C: 30.8 Tm: 70.2

### ComE region

#### ComE Primer Pair: F1-B1

[F1] 145-165 5'- CCTGAAAAGGGCAATCACCAAG -3'

21 nt forward primer

pct G+C: 52.4 Tm: 55.9

[B1] 606-585 5'- GCGATGGCACTGAAAAAGTCTC -3'

22 nt backward primer

pct G+C: 50.0 Tm: 55.4

462 nt product for F1-B1 pair (145-606)

Optimal annealing temp: 53.6

pct G+C: 38.3 Tm: 74.1

**Figure 9A**

Sequence Range: 1 to 2557

10            20            30            40            50  
ACATTATGTGCTTAAGAAAATTACTTTCAAGAAAATCCATGATT  
TGTAATACACAGGATTCTTATAATGAAAAAGTTCTTTAGGTACTAA  
              <K K L F I W S K  
              <\_\_\_\_\_>  
  
60            70            80            90            100  
TTTCATAAAAAATAGTATACTAATTATAATCAAAAAAGGAGATATAAA  
AAAAGTATTTTATCATATGATTAATATTAGTTCTCTATATTT  
              <K M F F L I S I I I L F L L Y L  
              <\_\_\_\_\_>  
  
110           120           130           140           150  
ATGAAAAAAACACTATCATTAAAAAATGACTTTAAAGAAATTAAGACTGA  
TACTTTTTGTGATAGTAATTTTACTGAAATTCTTAATTCTGACT  
M K K T L S L K N D F K E I K T D  
              ORF RF [2] >  
              <I F F V S D N F F S K L S I L V S  
              <\_\_\_\_\_>  
  
160           170           180           190           200  
TGAATTAGAGATTATCATTGGCGGAAGCGGAAGCCTATCACACATTCC  
ACTTAATCTCTAATAGTAACCGCCTTCGCCCTCGGATAGTTGAAAAAGG  
E L E I I I G G S G S L S T F F  
              ORF RF [2] >  
              <S N S I I M  
              <\_\_\_\_\_>  
  
210           220           230           240           250  
GGCTGTTAACAGAACAGTTTACACAAGCTTGGAAAATAAGATAGGCTA  
CCGACAAATTGCTTCAAATGTGTTGAAACCTTTATTCTATCCGAT  
R L F N R S F T Q A L G K  
              ORF RF [2] >  
  
260           270           280           290           300  
ACATTGGAATAAAACAAGGCTGGATTATTATTCCAGCCTTTAAATGT  
TGTAACCTTATTTGTTCCGACCTAATAATAAGGTCGGAAAATTACA  
  
310           320           330           340           350  
AAAATAAAAATACAGGGTTAATAATCAAGTGTGCTGCGATGAGAA  
TTTATTATTATGTCCAATTATTAGTTCACACGACAGCACCTACTCTT  
  
360           370           380           390           400  
GATAAAAATCTCTTAGAGAATAGGCCTCCTATTTATTAGGAG  
CTATTTGATAGAGAACATCTTATCCGGAGGAGATAAAATAATCCTC  
              <K I I L L  
              <\_\_\_\_\_ORF RF [\_\_\_\_\_>  
  
410           420           430           440           450  
TTGCTTGAATAAAATGATGATGATTGCTTGTAAACTGGTTGGAT  
AACGAACCTATTACTACTAACGAACAAACATTGACCAAAACCTA  
Q K F L H H N S T Q L S T K P Y

Figure 9B

< ORF RF [4] C >

460 470 480 490 500  
AATGTTCAAGAAATATGATTCACCTTGCTAAACCAATACCGCGATTGGAG  
TTACAAGTCTTATACTAAGTGGAAACGATTGGTTATGGCGCTAACCTC  
< H E L I H N V K A L G I G R N S  
< ORF RF [4] C >

510 520 530 540 550  
CCTTTAGTGGAAATAGTTTCTTAAAAATTTACTCACATCTATTGTT  
GGAAATCACCTTATCAAAAGAAAATTTAAAATGAGTGTAGATAAACAAA  
< G K T S Y N E K F I K S V D I Q K  
< ORF RF [4] C >

560 570 580 590 600  
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AAGAAACCACCTTAAGACTTACTATTTCTGATATGACGGTAAAAGAATT  
< E K T S N Q I I F V I S G N K K F  
< ORF RF [4] C >

610 620 630 640 650  
AAAAGGCTAACTGAATTTCAGGATTAAATGATTGAAAGCAGCCTCAATG  
TTTCCGATTGACTTAAAGTCCTAAATTACTAAGCTTCGTCGGAGTTAC  
M>  
>  
< F A L Q I E P N L S E F A A E I  
< ORF RF [4] C >

660 670 680 690 700  
GCATTATCACACAAGATAGAAAGTATGGTAATGAAATCAAGCAACTCCAT  
CGTAATAGTGTGTTCTATCTTCATACCATTACTTAGTCGTTGAGGTA  
A L S H K I E S M V M K S S N S I>  
ORF RF [3]>  
< A N D C L I S L I T I F D L L E M  
< ORF RF [4] C >

710 720 730 740 750  
CTCAGGCAGTTGTATTTACTTGAGACTTCTACATTGACAGCAATCTT  
GAGTCCGTCACATAAAATGAACCTCTGAAGATGTAACTGTCGTTAGAAA  
S G S C I L L E T S T L T A I F>  
ORF RF [3]>  
< E P L Q I K S S V E V N V A I K K  
< ORF RF [4] C >

760 770 780 790 800  
TATTCTGAGCTTCTAACAGATTTGCTGACAAGATAACCCCTGACAGCATCG  
ATAAGACTCGAAGATTCTAAAACGACTGTTCTATGGAACTGTCGTAGC  
L F>  
>  
< N Q A E L I K A S L I G K V A D  
< ORF RF [4] C >

810 820 830 840 850  
TTTGAATATTAGCTAGATGGCCGATATTATAACGGGTATCCTGCAATTG  
AAAACCTATAATCGATCTACCGGCTATAATATTGCCCATAGGACGTTAAC  
< N Q I N A L H G I N Y R T D Q L Q  
< ORF RF [4] C >

Figure 9C

860            870            880            890            900  
ATGTCCTTTCTAAGATTGATGGTAAATCTTCAATACTAGCTA  
TACAGGACAAAAAGATTCTAAACTACCATTAGAAAAGTTATGATCGAT  
**<H G T K E L I Q H Y I K E I S A L**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

910            920            930            940            950  
AATCTTATTTCAATGCCTAATCTGAGGCTAGTTAAAATATTAGATAA  
TTAGAAATAAAAGTTACGGATTAGACTCCGATCAATTATAAGTCTATT  
**<D K N E I G L R L S T L I N L Y**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

960            970            980            990            1000  
TCATGGCGAAACTTCGAATATCCTTGTAAGAGATTCTATTGCTGACT  
AGTACCGCCTTGAAGCTTATAGGAACATTCTCTAACGACTGA  
M A E T S N I L V K R F Y L L T >  
**<D H R F S R I D K Y L S E I Q Q S**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

1010           1020           1030           1040           1050  
ATACTGGGTGATATTCGAATCTGAGCTCCTTTGTGCCATTATCTCAT  
TATGACCCACTATAAGCTTAGACTCGAAGGAAACACGGTAATAGAGTA  
I L G D I S N L S F L L C H Y L I >  
**<Y Q T I N R I Q A E K Q A M I E N**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

1060           1070           1080           1090           1100  
TTGAACCTTTGTTGGTATATTGGCTAAAAATGAGATCAGAACAA  
AAACTGGAAAACAAACCATATAACCGAATTCTACTCTAGTCTAGTT  
L N L L F G I L A >  
**<Q V K Q K T Y Q S L F S I L I L**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

1110           1120           1130           1140           1150  
AATAAAATAAGATAGACAATAACGACAAATTACGAAATTAAAGTCGG  
TTATTTTATTCTATCTGTTATTGCTGTTAAATGCTTAAATTTCAGCC  
**<F L I L Y V I V V F K R F K L T P**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

1160           1170           1180           1190           1200  
TATCACATTATAACTCTCTATAACATACAATACCTGTATTAAAGGTAGT  
ATAGTGTAAATTGAGAGATATTGTATGGACATAATTTCATCA  
**<I V N Y S E I V Y L V Q I L L Y Y**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

1210           1220           1230           1240           1250  
ATAGAAGCATAGTAATATTCAATTGGAATCAAGCGTTTGACCTTCATC  
TATCTCGTATCATTATAAGTAACCTTAGTCGAAAAACTGGAAGTAG  
**<L L M T I N M P I L R K K V K M**  
**<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_**

1260           1270           1280           1290           1300  
TTGGTCAAACATCTTAAGTCGACCAATATCACACATTGAAACACTGAG

Figure 9D

AACCAAGTTGATAGAAATTCAAGCTGGTTATAGTTGTAACTTGTGTGACTC  
<K T L S D K L R G I D V N F V S L  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_

1310 1320 1330 1340 1350  
AAAGAGGTAACCTAGCGCTATTCCCTGCAAACTCGATCATATAGGTGGTTA  
TTTCTCCATTGAATCGCGATAAGGACGTTGAGCTAGTATATCCACCAAT  
<F L Y S L A I G A F E I M Y T T I  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_

1360 1370 1380 1390 1400  
TAATGCTACTGCCATTACAATTCCCTGAGTTCCATCCAAGATAAAGAAT  
ATTACGATGACGGGTAATGTTAAGGAACCTAAGGTAGGTTCTATTCTTA  
<I S S G M V I G Q T G D L I F F  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_  
<L E K L E M W S L S Y  
<\_\_\_\_\_

1410 1420 1430 1440 1450  
ATGATTGCCGCCTAACAAAGTCAGAACTGGCACAGGCAGCAGACCATA  
TACTAACGGCGGATTGTTAGTCTTGACCGTTGTCGTCGTCGTTGAT  
<I I A R R F L D S S A V P L L G Y  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_  
<S Q G G L C T L V P L L C C C V M  
<\_\_\_\_\_

1460 1470 1480 1490 1500  
AAATATATTAGAGAAAGACTATTCTGTCTATTAAGATAATTGATAAAG  
TTTATATAAATCTCTTCTGATAAGACAGATAATTCTATTAACTATTTC  
<F I N L S L S N Q R N L Y I S L A  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_

1510 1520 1530 1540 1550  
CTATAAAATAAAGAGGCTCTGCAGGATAAAACAGGTTACGTTACCATC  
GATATTTATTCCTCCGAGACGTCCTATTTGTCCTAAATGCAAGTGGTAG  
<I F Y L P E A P Y F L N V N V M  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_

1560 1570 1580 1590 1600  
GTAACAGCAATCATTATCAGAAAATTGCTTATCGAAAAAGAGTTAAC  
CATTGTCGTTAGTAATAGTCTTTAACGAATAGCTTTCTCAATTAAAG  
<T V A I M I L F N S I S F L T L E  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_

1610 1620 1630 1640 1650  
CTTTTCGATAAAAGTACATTACTACCTTAGAAAATAGAAACAAGAGAA  
GAAAAAGCTATTCACTGTAATGAAATGAACTTTATCTTGTCTCTT  
<K K S L T V N S V K S F L F L L F  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_

1660 1670 1680 1690 1700  
ATAGAACGGTTAGATAAGTTAATAAACCAATTGAAAGTATCATTAGGCT  
TATCTGCCAATCTATTCAATTATTGGTAAACTTCATAGTAATTCCGA  
<L V T L Y T L L G N S L I M L A  
<\_\_\_\_\_ ORF RF[4] C \_\_\_\_\_

1710 1720 1730 1740 1750

Figure 9E

TCATTCACTTGCTCTCCTTGATCAGCAATCACAGCTCTCAGTTTGTG  
AGTAAGTAAAACGAGAGGAAACTAGTCGTTAGTGTGAGAGTCAAAACAA  
<E N M  
<  
<K A R R Q D A I V A R L K T  
<\_\_\_\_\_ ORF RF [5] C \_\_\_\_\_  
  
1760 1770 1780 1790 1800  
AACTTAGTCGTGAAATAAGACAAGACTTATTATTCGAAAATAGGCCAA  
TTGAATCAAGCACTTATTCTGTTCTGAATAATAAAGCTTTATCCGGTT  
<L K T R S I L C S K N N R F Y A L  
<\_\_\_\_\_ ORF RF [5] C \_\_\_\_\_  
  
1810 1820 1830 1840 1850  
GCGTTTTCCGATCAATAACGGTAATATTGGCAGGATTGACAATAAAAG  
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<R K K R D I R T I N A P N V I F S  
<\_\_\_\_\_ ORF RF [5] C \_\_\_\_\_  
  
1860 1870 1880 1890 1900  
AGCGATGGCACTGAAAAAGTCTCTTATCCATTAAACAATGTCAGTCATA  
TCGCTACCGTGACTTTTCAGAGAATAGGAAAATTGTTACAGTCAGTAT  
M A L K K S L I H F N N V S H >  
ORF RF [1] >  
<R H C Q F L R K D M K V I D T M  
<\_\_\_\_\_ ORF RF [5] C \_\_\_\_\_  
<V  
<\_\_\_\_\_  
  
1910 1920 1930 1940 1950  
CTGCCGTAGAATTCAATCCGTTCATCATAAGTATAAAGGCAGAGCTTATG  
GACGGCATCTTAAGTTAGGCAAGTAGTATTCAATTTCCGTCTCGAACATAC  
T A V E F N P F I I S I K A E L M >  
ORF RF [1] >  
<S G Y F E I R E D Y T Y L C L K H  
<\_\_\_\_\_ ORF RF [5] C \_\_\_\_\_  
<A T S N L G N M M L I F A S S I  
<\_\_\_\_\_ ORF RF [6] C \_\_\_\_\_  
  
1960 1970 1980 1990 2000  
GGCTGTTGAAGATGTTCAAAATACAGAATCTCAGAAAAGGGACCTGAA  
CCGACAACCTCTACAAAGTTATGTCTAGTCGTTCCCTGGACTT  
G C >  
<A T S S T E F Y L I E A F P V Q F  
<\_\_\_\_\_ ORF RF [5] C \_\_\_\_\_  
<P Q Q L H K L I C F R L L L S R F  
<\_\_\_\_\_ ORF RF [6] C \_\_\_\_\_  
2010 2020 2030 2040 2050  
ACTGAGTTTCAGATGAATGGAAAATAAAAGTCTCTGATTGACCATT  
TGACTCAAAGTCTACTTACCTTTATTTCAAGGAGACTAACTGGTAAG  
<Q T E S S H F I F L E E S Q G N  
<\_\_\_\_\_ ORF RF [5] C \_\_\_\_\_  
<S L K L H I S F L F N R Q N V M R  
<\_\_\_\_\_ ORF RF [6] C \_\_\_\_\_

Figure 9F

2060 2070 2080 2090 2100  
TTCTGGCTTTCCATAGCATAATACAGCGCTGATTCAATGCCGGTGGGA  
AAGACCGACAAAAGGTATCGTATTATGTCGCGACTAACGTTACGCCACCT  
<K Q S N E M A Y Y L A S E I R H S  
<\_\_\_\_\_ ORF RF[5] C \_\_\_\_\_  
<R A T K W L M  
<\_\_\_\_\_ ORF RF[6] C \_\_\_\_\_

2110 2120 2130 2140 2150  
GAACTCCTCAGGATTCAAAGATTATCAATAAAATCCAAAGCAGATACCT  
CTTGAGGAGTCCTAAGTTCTAAATAGTTATTTAGGTTCTGCTATGGA  
<F E E P N L S K D I F D L A S V Q  
<\_\_\_\_\_ ORF RF[5] C \_\_\_\_\_

2160 2170 2180 2190 2200  
GATACTGAAAAGTGAGGGGCATAAACTCAGAATGTGTCGTGACAAAGACA  
CTATGACTTTCACTCCCCGTATTCAGTCTTACACAGCACTGTTCTGT  
M C R D K D >  
<Y Q F T L P M F E S H T T V F V  
<\_\_\_\_\_ ORF RF[5] C \_\_\_\_\_

2210 2220 2230 2240 2250  
ATAACTGCACTAGGATTATGCTGCTAACTGATTGGCTACTCCAGTCC  
TATTGACGTGATCCTAATACGACAGATTAGACTAACCGATGAAGGTAGG  
N N C T R I M L S N L I G Y F Q S >  
<I V A S P N H Q R I Q N A V E L G  
<\_\_\_\_\_ ORF RF[5] C \_\_\_\_\_

2260 2270 2280 2290 2300  
TTCTTTCCCTTTTGATTCAATATCCAAAAAGAAAATCTGGTGAT  
AAAGAAAAGGAGAAAAACTAAAGTTAGGTTCTTTAGACCACTA  
F L F L F F D F N I Q K E N L V I >  
<K K E E K K I E I D L F F I Q H N  
<\_\_\_\_\_ ORF RF[5] C \_\_\_\_\_

2310 2320 2330 2340 2350  
TGCCCTTTCAAGGATAGCGTCAATAAGTTGTTGTGGTTCCAAAAATA  
ACGGGAAAAGTCCCTATCGCAGTTATTCAACAAACACCAAAAGGTTTAT  
A L F R D S V N K L L W F S K N >  
<G K E E P I A D I L Q Q P K G F I  
<\_\_\_\_\_ ORF RF[5] C \_\_\_\_\_

2360 2370 2380 2390 2400  
GTCAATTCTTATAAGACCAATTCTTCTTCTGATGAGCTGCAATGGT  
CAGTTAAGAAAATATTCTGGTAAAAAAAGAAAAGTACTATCGACGTTACCA  
S Q F F I R P I F F H D S C N G >  
<T L E K Y S W N K E K M I A A I T  
<\_\_\_\_\_ ORF RF[5] C \_\_\_\_\_

2410 2420 2430 2440 2450

Figure 9G

GGTTTCAAGACGTCCTTGTGAAAAATCATCTTCCAATACAAAAATAG  
CCAAAGTTCTGCAGGAACAACATTTTAGTAGAAGGTTATGTTTTATC  
G F K T S L L>  
V S R R P C C K K S S S N T K I>  
< T E L R G Q Q L F D D E L V F I S >  
< ORF RF[5] C >  
2460 2470 2480 2490 2500  
AAATCATTATTCTCCTTAATCTCTATTAGGTTAGCTGATTAACACT  
TTTAGTAATAAGAGGAAATTAGAAGATAAATCCAATCGACTAATTGTGA  
E I I I S P L I F Y L G>  
< I M >  
2510 2520 2530 2540 2550  
ATACACAGAAAAGGTATAAACGATATCACTCAATAAAATCTACTAACTT  
TATGTGTCTTTCCATTTGCTATAGTGAGTTAGATGATTGAA  
AATAACC  
TTATTGG

Figure 10

A.

ATGGAAGAAGATTGTAAATAAGGTAAGCCAATTGTATGGAAATTAAG  
CCGTTATTACTTATTAAAATGTGGACTCGTGAAGATTGGCAACAAGAGGAATGTTGA  
TTTGCAACCAATTATTAAGGAAACATCCAGAATTAGAACAGGAGTATACAAAATTGTAT  
ATCTATTAAAGACACGTTTCTAATTACATTAAAGATGTTGCCTCAGCAAGAAAG  
TCAGAAACGTCGTTAAATAGAACATGTCTATGAAGAACGTCGGTAGATTGAAACACTGTT  
TGTCAAGTGGCGGTATGCAATTGGATGAATATATTTATTCTGTATAGTTGCTTGCA  
TATAAACAAAGGCTGAGTACTGAAAAGCAAGAGCTGTTGAGCGCTGGTAGCAGGAGA  
GCACTTTGGGAAGGCAAAGTATGCTGAAAGATTACGTAAAAATTAAAGTGATTTA  
AGGAAAAA

B.

MEEDFEIVFNKVKPIVWKLSRYYFIKMWTREDWQQEGMLILHQLLREHPELEEDDTKLY  
IYFKTRFSNYIKDVLRQQESQKRRFNRMSYEEVGEIEHCLSSGMQLDEYILFRDSLIA  
YKQGLSTEKQELFERLVAGEHFLGRQSMLKDLRKQLSDFKEK

C.

GTAAATAAAACAGCCAGTTAACAGATGGGACATTATGTCCTGTTAAAGTCTTTCG  
TTTATAATAATTATTATAAAAGGAGTCATCGTAATAGATGGAAGAACATTGAA  
ATTGTTTAAATAAGGTTAACGCAATTGATGGAATTAGCCGTTATTACTTTATTAA  
AATGTGGACTCGTAAGATTGCAACAAGAGGGATGTTGATTGACCAATTATTAA  
GGGAACATCCAGAATTAGAACAGGAGTACAAAATTGTATATCTATTAAAGACACGT  
TTTCTAATTACATTAAAGATGTTGCGTCAGCAAGAACGTCAGAAACGTCGTTAA  
TAGAAATGTCTTATGAAGAACGTCGGTAGATTGAACACTGTTGTCAGTGGCGGTATGC  
AATTGGATGAATATATTATTCTGTGATAGTTGCTGCAATAAACAAAGGTCTGAGT  
ACTGAAAAGCAAGAGCTGTTGAGCGCTGGTAGCAGGAGAGCACTTTGGGAAGGCA  
AAGTATGCTGAAAGATTACGTAAAAATTAAAGTGAATTAAAGGAAAAATAGTTAAAA  
GGGAAAGAATGGAACATGTGATTGTACCATCTTTGGTTGAAATTAAAGAAAAGTTA  
TTATAAATTATTGGTTAACATGCCATATTA

**Figure 11A.**

ATGAAACAAAGTATTTATGTTGTTTAATCGTCATGCCGTTAACATTCTCTTAGAGATT  
ATCAAAAGAGTAACAAAAGGGGAGGGACAGTTCGTCATCTAACCTTACCAAGATGGG  
CAGTCTAAGTTGTTGGCGCAGACATTATAAGCTAGTACCTCAGATTGATACCAGAGAC  
TGTGGCCGGCAGTGTGGCATCTGTTGCAAAGCATTACGGATCTAATTACTCTATCGCT  
TATCTCGGGAACTCTCAAAGACTAACAGCAGGGAACAAACAGCTTGGCATTGTTGAA  
GCTGCTAAAAAGTTAGGCTTGAAACACGCTCTATCAAGGCGGATATGACGCTTTGAT  
TATAATGATTGACCTATCCTTTATCGTCATGTGATTAAAGGAAAACGTCAGCAGCAT  
TATTATGTCGTCATGGCAGCCAGAATAATCAGCTGATTATTGGAGATCCTGATCCTCA  
GTTAAGGTGACTAGGATGAGTAAGGAACGCTTCAATCAGAGTGGACAGGCCTGCAATT  
TTCCTAGCTCCTCAGCCTAACTATAAGCCTCATAAAGGTGAAAAAAATGGTTGTCTAAT  
TTCTCCCGTTGATCTTAAGCAGAAAGCTTGATGACTTATATTATCATAGCTAGCTTG  
ATTGTGACGCTCATTGATATTGTCGGATCATACTATCTCCAAGGAATATTGGACGAGTAC  
ATTCCCTGATCAGCTGATTCAACTTAGGAATGATTACGATTGGCTGATAATAACCTAT  
ATTATCCAGCAGGTATGGCTTGCAAAAGAACATACCTCTGGCGTACTCAGTTGCGT  
TTAGTCATTGATGTTATCCTGTCTTATATCAAACATATTTTACGCTTCTATGTCTTC  
TTTGCACAAGGCGAACAGGAGAAATCACGTCTCGTTACAGATGCCAATCAGATTATT  
GATGCTGTAGCGTCAACCACCTTTCAATCTTTAGATATGACTATGGTAATTGGTT  
GGTGGGGTTTGTGGCGAAAACAATAACCTTTCTAACCTGCTCTCCATTCCG  
ATTATGCCATCATTATTTGCTTCTTGAAACCCCTTGAGAAAATGAATCACGAAGTG  
ATGGAAAGCAATGCTGGTAAGTCTCTATCATTGAAGATATCAATGGGATGGAAACC  
ATTAAATCACTACAAGTGAGTCCGCTCGTTATCAAACATTGATAGTGAATTGTTGAT  
TATTGGAGAAAAACTTTAAGCTACACAAGTATAGTGCCTTCAAAACCGCATTAAAAGC  
GGTGCTAAGCTATCCTCAATGTTGTCATTCTCTGGTATGGCTCTCGTCTAGTTATGGAT  
AATAAAATCTCAGTTGGTCAGCTTACACCTTAAATGCTTGTCTTATTTCTCAAAT  
CCAATTGAAAATATTATCAATCTGCAATCCAAACTGCAGTCAGCTCGCGTTGCCAATACA  
CGCTTAATGAGGTCTATCTGTCGAATCTGAATTGAAAAAGACGGCATTATCAGAA  
AATAGCTTTAGATGGTGATATTCGTTGAAAATCTTCTTATAAAATATGGATTGGG  
CGAGATACCTTACAGATATTAATTATCAATCAAAAAGGCTCAAGGTAGTCTAGTT  
GGAGCCAGTGGTCTGGTAAAACAACCTTGGCTAAACTGATTGTCATTCTACGAGCCT  
AACAAAGGGATTGTTCGAATCAATGGCAATGATTAAAAGTTATTGATAAGACAGCTTG  
CGCGGCATATTAGCTATTGCGCAACAGGCCTATGTTTAGTGGCTCTATTATGGAT  
AATCTCGTTTAGGAGCTAAAGAAGGAACGGAGTCAGGAAGACATTATTCGTGCTTGTGAA  
ATTGCTGAAATCCGCTCGGACATTGAACAAATGCCTCAGGGCTATCAGACAGAGTTATCA  
GATGGTGCCGGTATTCTGGCGGTAAAACAGCGGATTGCTTAGTGGCCTTATTA  
ACACAGGCACCGGTTTGATTCTGGATGAAGCCACCAGCAGTCTGATATTGACAGAA  
AAGAAAATTATCAGCAATCTCTTACAGATGACGGAGAAAACAATAATTGGCCAC  
CGCTTAAGCATTTCACAGCGTACTGACGAAGTCATTGTCATGGATCAGGGAAAAATTGTT  
GAACAAGGCACTATAAGGAACCTTAGCTAAGCAAGGTTCTATTATAACCTGTTAAT

**Figure 11B.**

MKQVIYVVLIVIAVNILLEIIKRVTKRGGTVSSNPLPDGQSCLFWRRHYKLVPQIDTRD  
CGPAVLASVAKHYGSNSIAYLRELSKTNQGTTALGIVEAAKKLGFETRSIKADMTLFD  
YNDLTYPFIHVIKGKRLQHYYVYGSQNNQLIIGDPDPSVKVTRMSKERFQSEWTGLAI  
FLAPQPQNYKPHGEKNGLSNFFPLIFKQKALMTYIIIASLIVTLIDIVGSYLYQGILDEY  
IPDQLISTLGMITIGLIITYIIQQVMAFAKEYLLAVSLRLVIDVILSYIKHIFTLPMSF  
FATRRTGEITSRFTDANQIIDAVASTIFSIFLDMTMVLVGGVLLAQNNNLFLTLLSIP  
IYAIIFIABLKPFEKMNHHEVMESNAVSSSIIEDINGMETIKSLTSESARYQNIDSEFVD  
YLEKNFKLHKYSAIQTALKSGAKLILNVVILWYGSRLVMDNKISVGQLITFNALLSYFSN  
PIENIINLQSKLQSARVANTRLNEVYLVESEFEKDGDLENSFLDGDISFENLSYKYGFG  
RDTLS DINLS IKKGSKVSLVGASGSGKTTLAKLIVNFYEPNKGIVRINGNDLKVIDKTAL  
RRHIS YLPQQAYVFSGSIMDNLVLAKEGTSQEDIIRACEIAEIRS DIEQMPQGYQTELS  
DGAGISGGQKQRRIALARALLTQAPVLILDEATSSL DILTEKKIIISNLLQMTEKTIIFVAH  
RLSISQRTDEVIVMDQGKIVEQGTHKELLAKQGFYYNLFN

**Figure 11C.**

ATGGATCCTAAATTTCACAAAGTCAGAATTAGGAGACGCTATCATAATTGCG  
ACACTATTAATTGTTCCCTTGGCTGCTTGATTATCTTCTGGCATATTCCCTTGT  
GCTAAAAAGAAATTACAGTGATTCTACTGGTGAAGTTGCACCAACAAAGGGTAGAT  
GTTATCCAATCTTACAGTGACAGTTCAATCATTAAAATAATTAGATAATAATGCAGCT  
GTTGAGAAGGGAGACGTTTAATTGAATATTCA GAAAATGCCAGTCCAAACCGTCAGACT  
GAACAAAAGAATATTATAAAAGAAAGACAAAACGAGAAGAGAAGGAAAAGAAAAACAC  
CAAAGAGCAAGAAAAAGAAGAAGTCTAACAGCAAGAAAGCTCCAAAGATAAGAAAAG  
AAATCGAAAGACAAGGAAAGCAGCTCTGACGATGAAAATGAGACAAAAAGGTTGATT  
TTTGCTTCAGAAGATGGTATTATTCAACCAATCCAAATATGATGGTGC  
CCGAAGCAAACCGAGATTGCTCAAATCTATCCTGATATTCAAAAACAAGAAAAGTTA  
ATCACCTATTATGCTTCTGATGATGTTGTTCTATGAAAAGGGCAAACCGCTCGT  
CTTCCCTGGAAAAAGGGAAATGACAAGGTTATTGAAGGAAAATTAACAATGTC  
GCTTCATCAGCAACTACTAAAAAGGAAATCTTTAAGGTTACTGCCAAAGTAAAG  
GTTTCTAAGAAAAATAGCAAACCATCAAGTATGGTATGACAGGCAAGACAGTC  
ATTGATAAAAAGACTTATTGATTATTCAAAGATAATTACTGCATAAAATGGATAAT

**Figure 11D.**

MDPKFLQSAEFYRRRYHNFATLLIVPLVCLIIFLVIFLCFAKKEITVISTGEVAPTKVVD  
VIQSYSDDSIIKNNLDNNAAVEKGDVIEYESNASPNRQTEQKNIKERQKREEKEKKH  
QKSKKKKSKSKASKDKKKSKDKESSSDDENETKKVSI FASEDGIHTNPKYDGANII  
PKQTEIAQIYPDIQKTRKVLITYYASSDDVVSMKKQATARLSLEKKNDKVIEGKINV  
ASSATTKKGNLFKVTAKVVKNSKLIKYGMTGKTVTVIDKKTYFDYFKDKLLHKMDN

Figure 12

